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March 9, 2000

Attorney Docket No.: 11544-003001

Box Patent Application
Assistant Commissioner for Patents
Washington, DC 20231

Presented for filing is a new original patent application of:

Applicant: FENG-NIEN KO, CHIEN-JEN SHIH, JE-YIE LIN, PEY-CHYI WU AND MO-CHI CHENG

Title: ANTI-ULCER PHARMACEUTICAL COMPOSITION AND THE PREPARATION THEREOF

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WASHINGTON, DC

Enclosed are the following papers, including those required to receive a filing date under 37 CFR 1.53(b):

	Pages
Specification	12
Claims	5
Abstract	1
Declaration	2

Enclosures:

- Assignment cover sheet and an assignment, 2 pages, and a separate $40 fee.
- Small entity statement. This application is entitled to small entity status.
- A certified copy of the priority application will be filed at a later date.
- Postcard.

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Typed or Printed Name of Person Signing Certificate

Under 35 USC 119, this application claims the benefit of a foreign priority application filed in Taiwan, serial number 89100334, filed January 11, 2000.

Basic filing fee	$345
Total claims in excess of 20 times $9	$18
Independent claims in excess of 3 times $39	$0
Fee for multiple dependent claims	$0
Total filing fee:	$363

A check for the filing fee is enclosed. Please apply any other required fees or any credits to deposit account 06-1050, referencing the attorney docket number shown above.

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Respectfully submitted,

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Enclosures
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Applicant or Patentee: Feng-Nien KO, Chien-Jen SHIH, Je-Yie LIN, Pey-Chyi WU and Mo-Chi CHENG

Attorney's Docket No.:

Serial or Patent No.: ____________

Filed or Issued: ____________

For: ANTI-ULCER PHARMACEUTICAL COMPOSITION AND THE PREPARATION

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) and 1.27 (d)) - NONPROFIT ORGANIZATION

I hereby declare that I am an official empowered to act on behalf of the nonprofit organization identified below:

NAME OF ORGANIZATION PHARMACEUTICAL INDUSTRY TECHNOLOGY AND DEVELOPMENT CENTER

ADDRESS OF ORGANIZATION 5F, NO. 101, LANE 169 KANG NING ST., HSI CHIH CITY, TAIPEI HSIEN, TAIWAN, R.O.C.

TYPE OF ORGANIZATION

( ) UNIVERSITY OR OTHER INSTITUTION OF HIGHER EDUCATION

( ) TAX EXEMPT UNDER INTERNAL REVENUE SERVICE CODE (26 USC 501(a) and 501(c)(3))

(X) NONPROFIT SCIENTIFIC OR EDUCATIONAL UNDER STATUTE OF STATE OF THE UNITED STATES OF AMERICA

(NAME OF STATE ____________)

(CITATION OF STATUTE ____________)

( ) WOULD QUALIFY AS TAX EXEMPT UNDER INTERNAL REVENUE SERVICE CODE (26 USC 501(a) and 501(c)(3)) IF LOCATED IN THE UNITED STATES OF AMERICA

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(NAME OF STATE ____________)

(CITATION OF STATUTE ____________)

I hereby declare that the nonprofit organization identified above qualifies as a nonprofit organization as defined in 37 CFR 1.9(e) for purposes of paying reduced fees under section 41(a) or (b) of Title 35, United States Code with regard to the invention entitled ANTI-ULCER PHARMACEUTICAL COMPOSITION AND THE PREPARATION by inventor(s) Feng-Nien KO, Chien-Jen SHIH, Je-Yie LIN, Pey-Chyi WU and Mo-Chi CHENG described in

(X) the specification filed herewith

( ) application serial no. ____________, filed ____________

( ) patent no. ____________, issued ____________.

I have declare that rights under contract or law have been conveyed to and remain with the nonprofit organization with regard to the above identified invention.

If the rights held by the nonprofit organization are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9(d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

*NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities (37 CFR 1.27)

NAME ____________

ADDRESS ____________

( ) INDIVIDUAL ( ) SMALL BUSINESS CONCERN ( )NONPROFIT ORGANIZATION

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( ) INDIVIDUAL ( ) SMALL BUSINESS CONCERN ( )NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING Shing-Tzuok TSAI

TITLE IN ORGANIZATION President

ADDRESS OF PERSON SIGNING 5F, NO. 101, LANE 169 KANG NING ST., HSI CHIH CITY, TAIPEI HSIEN, TAIWAN, R.O.C.

SIGNATURE [illegible] DATE Feb. 15, 2000

APPLICATION

FOR

UNITED STATES LETTERS PATENT

TITLE: ANTI-ULCER PHARMACEUTICAL COMPOSITION AND THE PREPARATION THEREOF

APPLICANT: FENG-NIEN KO, CHIEN-JEN SHIH, JE-YIE LIN, PEY-CHYI WU AND MO-CHI CHENG

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March 9, 2000
Date of Deposit

Christina Martinez
Signature

Christina Martinez
Typed or Printed Name of Person Signing Certificate

TITLE

ANTI-ULCER PHARMACEUTICAL COMPOSITION AND THE PREPARATION THEREOF

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to pharmaceutical compositions useful for the prevention and/or treatment of peptic ulcer diseases. More particularly, it relates to the use of American ginseng or the extract thereof as the active ingredient for the prevention and treatment of peptic ulcer diseases.

Description of the Related Arts

American ginseng (*Panax quinquefolium* L.) is one species of Araliaceae, which is the North American variety of ginseng native to the United States and Canada. The *Panax* plants in Araliaceae, such as *Panax ginseng*, *Panax quinquefolium*, *Panax pseudo-ginseng* etc, have been used as a form of tonic medicine in Chinese for a long period of time, and *Panax ginseng* is traditionally considered a valuable medicinal material in China, Japan and Korea. After harvesting, *Panax ginseng* with good quality is generally treated with boiling water or steam to give red ginseng. *Panax ginseng* which has been dried by hot air or sunlight is called white ginseng or unprocessed ginseng. The American ginseng is an herbaceous perennial and its root is mainly used as a nutritious tonic agent. Its morphology is similar to *Panax ginseng*, but has less fiber-like or lateral roots. At present, the American ginseng is artificially cultivated

in the United States, Mainland China and Russia. Many reports have shown some components of American ginseng are similar to *Panax ginseng*, including several kinds of ginseng saponins, oligosaccharides, volatile oils, amino acids, vitamins and trace elements. It is traditionally believed that both American ginseng and *Panax ginseng* possess effects of increasing physical strength, nourishing and preserving health, and prolonging life. Thus, they are regarded as mild tonics used for daily dietary or medicinal remedy.

Recently, a number of scientific reports show that the American ginseng indeed possesses a variety of physiological or pharmaceutical activities, including anti-aging (Xiao P.G. et. al., 1993, *Journal of Ethnopharmacology* **38**(2-3):167-75); preventing atherosclerosis and hyperlipidemia (Li J. et. al., 1999, *Life Science* **64**(1):53-62); protecting liver from injury (Yoshikawa M. et. al., 1998, *Chemical and Pharmaceutical Bulletin* **46**(4):647-54); enhancing the function of cardiovascular system (Kwan C. Y., 1995, *Clinical and Experimental Pharmacology and Physiology-Supplement* **1**:S297-9; Yang S., 1992, *China Journal of Chinese Material Medica* **17**(9):555-7 and US Patent No. 4,708,949); preventing memory dysfunction and dementia (Benishin C. G., 1991, *Pharmacology* **42**(4):223-9; Li Z. et. al., 1999, *Journal of Pharmacy and Pharmacology* **51**(4):435-40; Lewis R. et. al., 1999, *Phytotherapy Research* **13**(1):59-64); decreasing hyperglycemia (Oshima Y. et. al., 1987, *Journal of Natural Products* **50**(2):188-90; Martinez S. and Staba E. J., 1984, *Japanese Journal*

of Pharmacology **35**(2):79-85); inhibition of breast cancer cells (Duda R. B. et. al., 1996, *Annals of Surgical Oncology* **3**(6):515-20); enhancing physical strength; antiviral activity (US Patent No. 5,071,839); anti-oxidation; decreasing the side effects of anticancer chemotherapy and radiotherapy (US Patent No. 4,945,115); modulating gastric digestion (Yuan C. S. et. al., 1998, *American Journal of Chinese Medicine* **26**(1):47-55); and increasing the immune function (US Patent No. 4,795,742) etc.

Recently, the population with gastrointestinal diseases has been increasing, especially in highly developmental countries. The causes of peptic ulcers include unrelieved daily pressure; excessive alcohol irritation; the side effects of drugs, such as aspirin or non-steroid anti-inflammatory drugs; or *Helicobacter pyroli* infection. The predominant drugs used to treat peptic ulcers include muscarinic antagonists, such as methscopolamine bromide; H_2 blockers, such as cimetidine; antacids, such as aluminum hydroxide or magnesium hydroxide; H^+/K^+ ATPase inhibitor, such as omeprazole; anti-bacterial drugs, such as admixture of amoxicillin and metronidazole. Such drugs may be classified into two categories: one is used for physical protection of gastric mucosa to mitigate the irritation of the gastric acid to the mucosa ulcer site; the other is used for chemically inhibiting the secretion of the gastric acid, to avoid ulceration produced from excessive gastric acid erosion. The prevalence of peptic ulcers and

their high rate of recurrence may due to patients' life style or season change and many patients repeatedly suffer from peptic ulcers. Thus, there is a need for a safe, mild and effective drug for treating and preventing peptic ulcers.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide pharmaceutical compositions which are effective in preventing and/or treating peptic ulcer diseases, comprising an effective amount of American ginseng and/or the extract thereof, and a physiologically or pharmaceutically acceptable carrier.

An additional object of the present invention is to provide a process of preparing the extracts of the American ginseng described above, comprising the steps of (a) extracting American ginseng with a solvent with a polarity higher than 0.88 to obtain an extract; (b) filtering the extract to obtain a filtrate; and (c) centrifuging the filtrate to obtain a supernatant (total extract).

The preparation process according to the present invention may further comprise the means of ultrafiltrating, dialyzing, precipitating with ethanol, or performing reverse phase chromatography, to obtain certain fractions of American ginseng extract.

Another object of the present invention is to provide methods for preventing and/or treating a patient suffering from peptic ulcer, comprising administrating an effective amount of American ginseng and/or the extracts thereof to said patient.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention, there is provided a process of preparing the pharmaceutical compositions comprising American ginseng or the extract thereof. First, American ginseng is extracted with a solvent with a polarity higher than 0.88 to obtain an extract. Suitable solvent includes water, ethanol, methanol or the mixtures thereof, preferably water or ethanol, and more preferably 10% ~ 80% ethanol aqueous solution. Next, the extract is filtered to remove plant residues, and then centrifuged to remove microparticles and impurities. The resulting supernatant (total extract) is concentrated into an appropriate concentration, and then further treated by one or more of the following processes: ultrafiltrating, dialyzing, precipitating with ethanol, or performing reverse phase chromatography, to obtain various fractions of American ginseng extract.

In the process described above, ultrafiltrating is a step which the total extract is filtered by the ultrafiltration membrane with molecular weight cut off 1,000 or 3,000 to give a retentate and a filtrate. Dialyzing is a step in which the total extract is dialyzed by a membrane or dialysis bag with molecular weight cut off 500 to remove smaller molecules. Precipitating with ethanol is a step in which the filtrate obtained from ultrafiltration is concentrated to dry and then dissolved with 50% ~ 100% ethanol to obtain the soluble portion. Performing reverse phase chromatography is a step in which the filtrate obtained from ultrafiltration is loaded onto a reverse phase polyaromatic resin column, such as Diaion HP-20 (Sigma, Cat.

No. I-3605), to elute the active fraction of American ginseng extract.

All American ginseng extracts obtained from various processes of the present invention possess an anti-peptic ulcer effect. Moreover, these extracts may be added a physiologically acceptable carrier and/or formulated with a pharmaceutically acceptable excipient to obtain a pharmaceutical composition which is effective in treating or preventing peptic ulcers. The term "peptic ulcer" used hereinbefore and hereinafter refers to gastric ulcers and/or duodenal ulcers.

Without intending to limit it in any manner, the present invention will be further illustrated by the following examples which are associated with the design of the extraction step(s) and the assessment of pharmacological activity.

EXAMPLE 1

2,000 ml of deionized water was added to 200 g of chopped American ginseng and then heated to boil and further refluxed for 1 hour. The decoction was filtered through sieve gauge No. 200 (sieve pore 0.074 mm), and the filtrate (first filtrate) was collected. An additional 2,000 ml of deionized water was added to the residue of the American ginseng described above, and was refluxed and filtered as described above to give the second filtrate. These two filtrates were combined and centrifuged at 10,000 rpm for 30 minutes to remove microparticles and impurities. The supernatant (total extract) was then filtered through the ultrafiltration membrane with molecular weight cut off 1,000

(Amicon, Cat. No. S1Y1) to remove substances with molecular weight less than 1,000 dalton. The retentate containing substances with molecular weight greater than 1,000 dalton was concentrated under reduced pressure to give the extract I. The filtrate containing substances with molecular weight less than 1,000 dalton was concentrated to dry, and then 90% ethanol solution was added to dissolve those substances. The ethanol solution was filtered (Advantec No. 2) to obtain the soluble portion, and the resulting soluble portion was added into the extract I described above. The mixture was concentrated under reduced pressure to give the extract II.

EXAMPLE 2

The total extract described in EXAMPLE 1 was treated through an ultrafiltration membrane with molecular weight cut off 3,000 (Amicon, Cat. No. S1Y3) to remove substances with molecular weight less than 3,000 dalton. The retentate containing substances with molecular weight greater than 3,000 dalton was concentrated under reduced pressure to give the extract III. The filtrate containing substances with molecular weight less than 3,000 dalton was loaded onto a column packed with Diaion HP-20 resin (Sigma, Cat. No. I-3605). The column was first eluted with deionized water until the eluate was colorless, and then eluted with 95% ethanol and the eluate was collected. The 95% ethanol eluate was added into the extract III described above. The mixture was concentrated under reduced pressure to give the extract IV.

EXAMPLE 3

The total extract described in EXAMPLE 1 was loaded in a dialysis bag with molecular weight cut off 500 (Spectra/Por®, Cat. No. 131 057). Both ends of the bag were sealed with clamps. The bag was placed in a bucket contained deionized water, in which the ratio of the supernatant and deionized water was 1:10. The total extract was dialyzed at 4°C with stirring thrice each for 20 hours. The solution remaining in dialysis bag was collected and concentrated under reduced pressure to give the extract.

EXAMPLE 4

1,000 ml of 80% ethanol solution was added to 100 g of chopped American ginseng and was heated to boil and further refluxed for 1 hour. The decoction was filtered through sieve gauge No. 200, and the filtrate (first filtrate) was collected. An additional 1,000 ml of 80% ethanol solution was added to the residue of the ginseng and extracted as described above, to give the second filtrate. These two filtrates were combined and concentrated under reduced pressure to give the extract V.

EXAMPLE 5

Assessment of the pharmacological activity of anti-peptic ulcer:

The anti-peptic ulcer activity of American ginseng was assessed using the methods described by Robert A. et. al. (1979, *Gastroenterology* **77**:433-443), and Takagi I. and Okabe S. (1968, *Japan J. Pharmacol.* **18**:9-18), which is summarized below.

(1) The assessment of stress-induced ulcer:

Male Long Evans rats, weighing 150±20 g, were administrated American ginseng extracts orally after being fasted for 18 hours, while the control rats were administrated the same volume of distilled water orally. After 1 hour, the rats were placed in a holder and partially immersed in water at 22 ~ 24°C for 4 hours. The rats were then sacrificed and their stomachs were opened along the greater curvature for evaluation the degree of ulceration. Gastric ulceration was scored according to an arbitrary system:

0 = no bleeding
1 = spot bleeding
2 = slight bleeding
3 = severe bleeding and half stomach bloodstained
4 = very severe bleeding and entire stomach bloodstained

Table 1. Effect of American ginseng extracts on stress-induced ulcer in rat.

Treatment	Dose (g/kg)	N	Inhibition (%)[a]
Total Extract	4	10	27.5±2.4
Extract I	4	10	42.5±3.6
Extract II	4	6	37.5±5.1
Extract III	4	10	42.5±3.6
Extract IV	4	6	51.2±3.8
Extract V	4	4	37.5±6.3

a: The inhibition rate (%) is calculated by the following equation:

[(score of control animal)-(score of experimental animal)]/ (score of control animal) x 100%.

All the ulcer scores of the control rats were 4.

(2) The assessment of ethanol-induced ulcer:

Male Long Evans rats, weighing 150±20 g, were administrated American ginseng extracts orally after being fasted for 18 hours, while the control rats were administrated the same volume of distilled water orally. After 15 minutes, the rats were administered 1 ml of absolute ethanol. After 1 hour, the rats were sacrificed and gastric ulceration was scored according to an arbitrary system:

0 = no lesions
1 = hyperaemia
2 = one or two slight lesions
3 = more than two slight lesions or severe lesions
4 = very severe lesions

Table 2. Effect of American ginseng extract on ethanol-induced ulcer in rat.

Treatment	Dose (g/kg)	N	Inhibition (%)[a]
Total Extract	4	10	50.0±0.0
Extract I	4	10	50.0±0.0
Extract II	4	6	45.8±3.8
Extract III	4	10	40.0±5.2

a: The inhibition rate (%) is calculated by the following equation:
[(score of control animal)-(score of experimental animal)]/ (score of control animal) x 100%.
All the ulcer scores of the control rats were 4.

The results of pharmacological assessment shown in Tables 1 and 2 reveal that American ginseng extracts of the present invention possess excellent inhibition effects of gastric ulcers induced by stress and alcohol. In addition, according to the present invention, the American ginseng extracted with water or ethanol solution and further treated by ultrafiltration, dialysis, precipitation with ethanol, or

reverse phase chromatography, possesses excellent anti-peptic ulcer effects.

While the invention has been particularly shown and described with the reference to the preferred embodiment thereof, it will be understood by those skilled in the art that various changes in form and details may be made without departing from the spirit and scope of the invention.

WHAT IS CLAIMED IS:

1. A pharmaceutical composition for preventing and/or treating peptic ulcer, comprising:

(i) an effective amount of American ginseng and/or the extract thereof; and

(ii) a physiologically or pharmaceutically acceptable carrier or excipient.

2. The pharmaceutical composition according to claim 1, wherein said American ginseng is *Panax quinquefolium* L..

3. The pharmaceutical composition according to claim 1, wherein said American ginseng extract is extracted with a solvent having a polarity higher than 0.88.

4. The pharmaceutical composition according to claim 3, wherein said American ginseng extract is extracted with 10% ~ 80% ethanol aqueous solution.

5. The pharmaceutical composition according to claim 3, wherein said American ginseng extract is extracted with water.

6. The pharmaceutical composition according to claim 1, wherein said American ginseng extract is extracted with water or 10% ~ 80% ethanol aqueous solution, centrifuged, and filtered through an ultrafiltration membrane with molecular weight cut off 1,000 to give a retentate containing substances with molecular weight greater than

1,000 dalton, and the retentate being concentrated to give an extract I.

7. The pharmaceutical composition according to claim 6, wherein said American ginseng extract is extracted with water or 10% ~ 80% ethanol aqueous solution, centrifuged, and filtered through an ultrafiltration membrane with molecular weight cut off 1,000 to give a filtrate containing substances with molecular weight less than 1,000 dalton, the filtrate being concentrated to dry, added ethanol solution to dissolve said substances, filtered said ethanol solution to obtain a soluble portion, added said soluble portion into said extract I as claimed in claim 6 to obtain a mixture, and concentrated said mixture to give the extract II.

8. The pharmaceutical composition according to claim 1, wherein said American ginseng extract is extracted with water or 10% ~ 80% ethanol aqueous solution, centrifuged, filtered through an ultrafiltration membrane with molecular weight cut off 3,000 to give a retentate containing substances with molecular weight greater than 3,000 dalton, and the retentate being concentrated to give an extract III.

9. The pharmaceutical composition according to claim 8, wherein said American ginseng extract is extracted with water or 10% ~ 80% ethanol aqueous solution, centrifuged, filtered through an ultrafiltration membrane with molecular weight cut off 3,000 to give a filtrate containing substances with molecular weight less than 3,000 dalton, the filtrate being loaded onto a reverse phase column, eluted with water, followed by ethanol solution and collected the

eluate, and then the 95% ethanol is combined with said extract III in claim 8 and concentrated to give extract IV.

10. The pharmaceutical composition according to claim 1, wherein said American ginseng extract is extracted with 30% ~ 90% ethanol aqueous solution followed by filtration and concentration to give extract V.

11. The pharmaceutical composition according to claim 1, wherein said peptic ulcer is a gastric ulcer or duodenal ulcer.

12. A process of preparing an American ginseng extract for preventing and/or treating peptic ulcers, comprising the steps of:

(a) extracting American ginseng with a solvent with a polarity higher than 0.88 to obtain an extract;

(b) filtering said extract to obtain a filtrate; and

(c) centrifuging said filtrate and collecting the supernatant to give the total extract.

13. The process according to claim 12, further comprising the step of ultrafiltrating said total extract to give a retentate and a filtrate.

14. The process according to claim 13, wherein said ultrafiltrating is a step in which said total extract is filtered by means of an ultrafiltration membrane with molecular weight cut off 1,000 or 3,000 to remove smaller molecules.

15. The process according to claim 12, further comprising the step of dialyzing said total extract.

16. The process according to claim 15, wherein said dialyzing is a step in which said total extract is dialyzed by means of a dialysis membrane with molecular weight cut off 500 to remove smaller molecules.

17. The process according to claim 13, further comprising a precipitating step in which said filtrate is concentrated to dry and then dissolved with 50% ~ 100% ethanol to obtain the soluble portion.

18. The process according to claim 13, further comprising the step of performing reverse phase chromatography of said filtrate.

19. The process according to claim 18, wherein said reverse phase chromatography is performing with a reverse phase polyaromatic resin column.

20. The process according to claim 12, wherein said American ginseng extract is extracted with 10% ~ 80% ethanol aqueous solution.

21. The process according to claim 12, wherein said American ginseng extract is extracted with water.

22. A method for preventing and/or treating a patient suffering from peptic ulcer, comprising administrating an

effective amount of American ginseng and/or the extracts thereof to said patient.

Client's Ref.: PITDC-

File: 0641-5101-US/Final/Frank

TITLE

ANTI-ULCER PHARMACEUTICAL COMPOSITION AND THE PREPARATION THEREOF

ABSTRACT OF THE DISCLOSURE

The invention discloses a pharmaceutical composition for preventing and/or treating peptic ulcer, including American ginseng or the extract thereof, and a method for preparing American ginseng extract, said method including extracting American ginseng with water or ethanol aqueous solution, and then ultrafiltrating, dialyzing, precipitating with ethanol, or performing reverse phase chromatography to obtain various fractions of extract with anti-peptic ulcer effect.

PATENT

ATTORNEY DOCKET NO:

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled ANTI-ULCER PHARMACEUTICAL COMPOSITION AND THE PREPARATION the specification of which

- ■ is attached hereto.
- ☐ was filed on _____ as Application Serial No. _____ and was amended on _____.
- ☐ was described and claimed in PCT International Application No. _____ filed on _____ and as amended under PCT Article 19 on _____.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose all information I know to be material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application(s) of which priority is claimed:

COUNTRY	APPLICATION NO.	FILING DATE	PRIORITY CLAIMED
Taiwan, R.O.C.	89100334	11/01/2000	☒Yes ☐ No
			☐Yes ☐ No

I hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Eric L. Prahl, Reg. No. 32,590, and Y. Rocky Tsao, Reg. No. 34,053; Frank R. Occhiuti, Reg. No. 35,306.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

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PATENT

COMBINED DECLARATION AND POWER OF ATTORNEY

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Inventor's Signature: Chien-Jen Shih Date: Feb. 21, 2000

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Full Name of Inventor: Pey-Chyi WU

Inventor's Signature: Pey-Chyi Wu Date: Feb. 21, 2000

Residence Address: Same as Post Office Address (Below)

Citizen of: Taiwan, R.O.C.

Post Office Address: 1F, No. 9, Lane 146, Wan-Sheng St., Taipei, Taiwan, R.O.C.

Full Name of Inventor: Mo-Chi CHENG

Inventor's Signature: Mo-Chi Cheng Date: Feb. 21, 2000

Residence Address: Same as Post Office Address (Below)

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Full Name of Inventor: _____

Inventor's Signature: _____ Date: _____

Residence Address: _____

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